UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/849,664	05/19/2004	Aladar Szalay	17248-004002 (4804B)	7765

7590 03/12/2007

Stephanie Seidman
FISH & RICHARDSON P.C.
12390 El Camino Real
San Diego, CA 92130-2081

EXAMINER	
KELLY, ROBERT M	
ART UNIT	PAPER NUMBER
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/849,664	SZALAY ET AL.	
	Examiner	Art Unit	
	Robert M. Kelly	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 December 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-47 and 51-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-47 and 51-80* is/are rejected.

7)☒ Claim(s) *80* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 December 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: HTTP://WWW.ANSWERS.COM/TOPIC/BACTERIOPHAGE.

DETAILED ACTION

Applicant's response and amendment of 12/18/06 is entered.

Claims 48-50 have been cancelled.

Claim 80 has been newly added.

Claims 33-35 have been amended.

Claims 33-47 and 51-80 are presently pending.

Election/Restrictions

It is noted that no claim has been amended to comprise, and no new claim is presented which encompasses non-elected subject matter.

Hence, Claims 33-47 and 51-80 are presently considered.

Claim Status, Canceled Claims

In light of the cancellation of Claims 48-50, all objections and/or objections to such claims are rendered moot and thus, are withdrawn.

Drawings

In light of the amendments, the objections to drawings 6 and 7 are withdrawn.

To wit, Applicant has amended the drawing and the description such that the amendments overcome the objections.

Figures 1-7 appear to actually be color or black-and-white photographs, however,

Applicant has not filed a petition to enter color photographs, and as such, no consideration of any actual color photographs are considered, and such photographs may not copy into a patent that issues such that the pictures would be useful.

37 CFR 1.84(b) states:

(1) Black and white. Photographs, including photocopies of photographs, are not ordinarily permitted in utility and design patent applications. The Office will accept photographs in utility and design patent applications, however, if photographs are the only practicable medium for illustrating the claimed invention. For example, photographs or photomicrographs of: electrophoresis gels, blots (e.g., immunological, western, Southern, and northern), auto-radiographs, cell cultures (stained and unstained), histological tissue cross sections (stained and unstained), animals, plants, in vivo imaging, thin layer chromatography plates, crystalline structures, and, in a design patent application, ornamental effects, are acceptable. If the subject matter of the application admits of illustration by a drawing, the examiner may require a drawing in place of the photograph. The photographs must be of sufficient quality so that all details in the photographs are reproducible in the printed patent.

(2) Color photographs . Color photographs will be accepted in utility and design patent applications if the conditions for accepting color drawings and black and white photographs have been satisfied. See paragraphs (a)(2) and (b)(1) of this section.

As is noted, the Examiner is unsure if such drawings are actually color or black-and-white photographs. Either way, if Applicant does wish photographs to be present in the specification of any patent that may issue from this Application, Applicant is requested to comply with 37 CFR 1.84.

Claim Objections

In light of Applicant's argument, the objections to Claims 61-63 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, are withdrawn.

It is noted that such objection is typically used to indicate that the dependent claim is broader than the parent claim, and not for having the exact same scope.

Claim 80 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 80 is limited to disorders/conditions which are no longer in the Markush group listed in its parent claim, Claim 35.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Applicant is again advised that should claims 33, 34, and/or 35 be found allowable, claims 61, 62, and/or 63, respectively, will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof, for reasons of record. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Response to Argument – Double Patenting

Applicant's argument of 12/18/06 has been fully considered, but is not found persuasive.

Applicant argues that the signal is distinct from that of visualization, and as such, visualization may be made without a signal (pp. 10-13).

Such is not persuasive. As has been stated, no detection can be made without, or as Applicant recites "based on", as signal. If there is no signal, whether it is light bouncing off an organism, sound, or other form of energy that produces the detection, there is no detection. Hence, in Applicant's argument, the light bouncing off of something is a signal, and it is not simply detected without that light signal. Further, arguments that the Artisan would know the difference is not sufficient, as the broadest reasonable interpretation of the claims is that Applicant is claiming detection, by any method, which requires a signal. There is no Art recognized "based on a signal" detection which is distinct from that which is "not based on a signal".

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting

ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 33-47, 51-80 remain, or are newly provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 3-19 of copending Application No. 10/516,785, for reasons of record. Although the conflicting claims are not identical, they are not patentably distinct from each other because Applicant's copending Application teaches broadly the cell/microorganism, and methods of diagnosis, and the specification of Application No. 10/516,785 is substantially identical to the present specification, describing the same uses; and while Application No. 10/516,785 may only broadly claim use, the specification then necessarily teaches the same invention claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Argument – Double Patenting

Applicant argues that these rejections should be held in abeyance, and addressed if these claims are found otherwise allowable (p. 12).

Such is acceptable. The Examiner will not address these rejections until such time as the claims are found allowable.

Claim Rejections - 35 USC § 112 – new matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of the amendments, the rejections of Claims 33-46 and 51-80 remain and/or are newly rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It is noted that that scope of this rejection for lacking a nexus between the administration of the microorganism/bacteria and the detection, are withdrawn, **however, the balance of the rejection remains: that basis drawn to microorganisms/bacteria not containing a DNA sequence capable of inducing a detectable signal, for reasons of record.**

Response to Argument – New Matter

Applicant's argument of 12/18/06 has been fully considered and not found persuasive.

Applicant's argument is that specific paragraphs within the specification when taken out of the context of the whole of the specification, and placed in comparison to one another demonstrate that the DNA encoding the protein does not have to encode a protein capable of inducing a detectable signal (p. 18).

Such is not persuasive. At no point in the specification is there even mention of an absence of a DNA encoding a protein in the microorganism/bacteria. Also, the confluence of the specification would only convey to the Artisan that Applicant considered the DNA essential to the detection, and further, because there is no other use for this DNA sequence but to aid in detection, The Artisan similarly could not conclude that Applicant considered the invention to be

any microorganism/bacteria capable of detection without use of a DNA encoding a protein capable of inducing a detectable signal. Lastly, if Applicant is arguing that the detectable signal is again not required, such is simply not the case, as a signal is required to be detected, to see the microorganism/bacteria by any specific means.

***

Claim Rejections - 35 USC § 112 – New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35, 38-39, 44, 47, 50, 53, 56, 63, 66, 73, 76, and 79 remain, and Claim 80 is newly, rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's claims encompass the diagnosis of low back pain, as well as herniated nucleus pulposis. However, Applicant's specification and claims as orginially filed only provide support for low back pain which **is** herniated nucleus pulposis (e.g., paragraph 0046 and claim 21). Hence, the claims encompass new matter.

Response to Argument – New Matter

Applicant's argument of 12/18/06 has been fully considered but is not found persuasive.

Applicant argues that they have amended the claims to overcome the rejection (p. 13).

Such is not persuasive. As has been stated, Applicant only discloses herniated nucleus pulposis as being the same scope as that of low back pain (see repeat of rejection, above). Hence, by moving herniated nucleus pulposis to a dependent claim, Applicant is now not only claiming herniated nucleus pulposis as distinct from that low back pain, but claiming that low back pain has a larger scope than that evinced to be contemplated by Applicant's disclosure in their original claims and specification. Hence, these claims remain rejected for reasons of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35, 38-39, 44, 47, 53, 56, 63, 66, 73, 76, and 79 remain, and Claim 80 is newly, rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant's claims encompass the diagnosis of Crohn's disease, ulcerative colitis, atherosclerotic plaque, auto-immune disease, rheumatoid arthritis, multiple sclerosis, Alzheimer's disease, a fracture, an incision, and a burn. However, the specification and claims

as originally-filed do not support these disorders for anything but treatment (e.g., paragraph 0046). Hence, the claims encompass new matter.

Response to Argument – new matter

Applicant's argument of 12/18/06 has been fully considered but is not found persuasive.

Applicant argues that the treatment and the diagnosis follow the same routine, and therefore, by specifically disclosing the treatment of a disease, the diagnosis is necessarily disclosed (pp. 16-17).

Such is not persuasive. Applicant is basically arguing that, from the disclosure, the various diagnoses are obvious, as one could extrapolate from the disclosure to do such. However, obviousness does not suffice for written description, and there is no specific contemplation of these disorders for diagnosis in the specification and claims as originally filed. Hence, the claims remain, and/or are newly, rejected for comprising new matter.

Claim Rejections - 35 USC § 112 – written description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In light of the amendments, the rejections of Claims 33-47 and 51-79 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, are withdrawn. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To wit, Applicant has amended the claims to be limited to non-pathogenic or attenuated microorganisms/cells, as well as being recognized by the immune system of the patient.

Claim Rejections - 35 USC § 112 – Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33-47 and 51-79 remain, and Claim 80 is newly, rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The Law

In determining whether Applicant's claims are enabled, it must be found that one of skill in the art at the time of invention by Applicant would not have had to perform "undue experimentation" to make and/or use the invention claimed. Such a determination is not a simple factual consideration, but is a conclusion reached by weighing at least eight factors as set forth in In re Wands, 858 F.2d at 737, 8 USPQ.2d at 1404. Such factors are:

(1) The breadth of the claims;

(2) The nature of the invention;

(3) The state of the art;

(4) The level of one of ordinary skill in the art;

(5) The level of predictability in the art;

(6) The amount of direction and guidance provided by Applicant;

(7) The existence of working examples; and

(8) The quantity of experimentation needed to make and/or use the invention.

These factors will be analyzed, in turn, to demonstrate that one of ordinary skill in the art would have had to perform such experimentation as to amount to inventing Applicant's claimed subject matter for Applicant, and hence Applicant's claimed subject matter requires "undue experimentation" to make and/or use the invention, and that, therefore, Applicant's claims are not enabled.

The Level of Predictability in the Art

Because of the art, as shown above, does not disclose enough to reasonably predict the working embodiments encompassed by Applicant's claims, the Artisan could not predict, in the absence of proof to the contrary, that such applications would efficacious in any diagnosis, as will be shown below.

Hence, absent a strong showing by Applicant, in the way of specific guidance and direction, and/or working examples demonstrating the same, such invention as claimed by Applicant is not enabled.

The Level of One of Ordinary Skill in the Art at the Time of Invention

The level of one of ordinary skill in the art at the time of invention was advanced, being that of a person holding a Ph.D. or an M.D.; however, because of the immaturity of the art, and its unpredictability, as shown by the other factors, one of skill in the art at the time of invention

by Applicant would not have been able to make and/or use the invention claimed without undue experimentation.

The Breadth of the Claims

Applicant's independent claims are drawn to detecting the presence or absence of a wound/wounded tissue, inflammation site/tissue, or a disease/condition, in a subject (Claims 33-35, respectively). Each claim requires monitoring a subject to whom any detectable microorganism or cell has been has been administered, to detect the microorganism/cell, and thereby detect the wound/tissue/inflammation/disease/condition, respectively, in the same subject. Dependent claims encompass microorganisms that are any bacteria, the condition being an atherosclerotic plaque, the cell being specifically retained at the wound/wounded tissue or inflammation site/inflamed tissue due to protection from the immune system and further being cleared without affecting normal tissues. Further dependent claims encompass any microorganism/cell which is capable of replication, intravenous administration, attenuated or non-pathogenic microorganisms, four genera and species of bacteria, the microorganism allowing for visualization and external visualization of the wounded/inflamed tissues, detection being based on a signal, signals of MRI, cells comprising a DNA encoding a contrast agent, chromophore, compound, or ligands for visualization, cells allowing detection via light, heterologous genes encoding fluorescent proteins, luminescent proteins, metal binding proteins, luciferase and/or its substrate, GFP or RFP.

The claims are broad for encompassing a wide variety of subjects, tissues, diseases, cells, microorganisms, and detection methods. The breadth encompassed requires a large amount of information to be provided by Applicant's specification and examples, and the Art at the time of

filing, for the Artisan to reasonably predict the working embodiments encompassed by the breadth of the invention.

The Nature of the Invention

Applicant's invention is in the nature of detecting wounded tissues, inflamed tissues, or diseases/conditions, by the administration of any microorganism or cell and detecting their accumulation in the tissues affected (e.g., paragraph 0023). However, Applicant's claims appear to require separate detections of the microorganism or cell, and the tissue affected, and hence, there appears to be no direction and/or guidance for the presently claimed method. Hence, the Artisan would have to perform undue experimentation to determine the methods of detection, because the methods of detection would not reasonably predictable.

The State of the Prior Art

Dr. Szalay's own article, Yu, et al. (2003) Anal. Bioanal. Chem., 377: 964-72, provides a recent review of the Art, demonstrating that the Art is not generally enabling of the breadth of Applicant's invention. Specifically, Yu is directed to the administration of bacteria, viruses, or mammalian cells (BVMC) to subjects, which BVMC accumulates in cancerous tissues, and not any tissue of the claimed invention.

With regard to bacterial cells, Yu teaches a few species of bacteria which appear to preferentially colonize cancerous tissues, but the mechanism of such colonization, while proposed to be due to various things, is not yet elucidated (pp. 966-67). Moreover, a particular mouse was found that showed a very short term accumulation of bacteria which disappeared prior to full disappearance of the bacteria in a particular mouse strain (p. 966). Further, Yu discloses that administration-type-dependent colonization is common, but there appears to be no

reasoning to predict which administration will yield which colonization type (p. 966, paragraph bridging columns).

The Direction and Guidance Provided by Applicant

Applicant's specification broadly discusses bacteremias and possible reasons why bacteria may colonize artificial materials in the body (pp. 1-3), a summary of the invention broadly discusses monitoring the colonization of bacteria in the body non-invasively, which is preferentially carried out with Applicant's Luxcdabe operon (pp. 3-4). Further broad description is provided stating that S. typhimurium disemminates through intravenous injection throughout the body, and may therefore reach the wounded/inflamed tissue by circulation (p. 6), broad description of the envisioned cell types, tissues, administrations, heterologous genes for therapy, discussion of luciferases, promoters, administrations, therapeutic use, and therapeutic proteins (pp. 7-14).

However, such broad description fails to provide the specific guidance and direction required to reasonably predict that any particular subject, tissues, diseases, cells, microorganisms, and detection methods, would be efficacious.

The Existence of Working Examples

Example 1 demonstrates the materials and methods used in the subsequent experiments. Example 2 demonstrates that distributions of bacteria into the body after administration are bacterial-strain dependent. Further, V. cholera appears to localized to the liver, within 5 minutes of injection, and remains visible in the liver at the one-hour period. The next experiment demonstrates that at 5 days, the cholera is cleared from the ear tag wound, and at 8 days, even the injection wound site is cleared of cholera. Next, it was demonstrated that in immunocompetent

mice, ear tags were colonized four days after intravenous injection. Lastly, it was found that 24 of 29 injection wounds, and 12 of 29 ear tags were colonized by cholera. Example 3 demonstrates that E coli injected intravenously appear to colonize catheter-irritated hearts of rats, while those that are not so-irritated are unaffected, and the catheters are not affected.

The Amount of Experimentation to Practice the Invention

Applicant's examples and specification are not consistent, given the knowledge in the art, to the breadth of Applicant's claims. With regard to the microorganisms which may be administered, the Artisan would not reasonably predict that any microorganism would accumulate in any of the tissues claimed. To wit, for example, a bacteriophage cannot even infect eukaryotic cells, and hence would not be reasonably predicted to accumulate anywhere except the liver. Further, Applicant has stated in the specification that even the bacteria used to infect the rats used have distinct interactions with the host cell (paragraph 0061), and the distribution pattern of any particular bacteria is not reasonably predictable, being bacterial-strain dependent (paragraph 0060), and, moreover, the particular distribution patterns depends on the method of administration (paragraph 0045). Hence, any microorganism's exposure to any particular tissue, and its clearance, is not reasonably predictable. Given this, and given the number of microorganisms and cells and animals and forms of administration that are possible, the Artisan would have to perform undue experimentation to determine for each type of microorganism or cell, and each subject type, first, whether the administration yields the distribution which will yield positive results, and then determine when and where, by comparison to the non-affected subject, the colonization is different in the diagnosed subject. For example, by Applicant's method, if a rat was unaffected, accumulation in the liver would

indicate that the liver had a wound, inflammation, and coronary artery disease. This simply is not the case, as it is the artifact of the nature distribution of the bacteria used. Further, given that the colonizations are not permanent and do not necessarily occur immediately, as shown in the Yu article, above, as well as Applicant disclosure (paragraph 0061), the Artisan would have to determine the distribution over time for a non-affected individual for comparison, prior to performing the method, and may still only expect the method to be accurate, at best, only 41.4% of the time (paragraph 0061). Applicant may argue that 82.8% of injection wounds also showed such colonization, but such may also be explained by the fact that such is where the bacteria was present in high concentrations, and hence, it would not be reasonably predictable for non-injection wounds, and therefore would require undue experimentation for the breadth to make it so-predictable.

With regard to Applicant's detection methods, the specification only discloses fluorescent proteins, for detection by light emission, and by MRI, (e.g., p. 8). However, Applicant's claims encompass any detection method. However, given that Applicant wishes to detect these tissues, the method would not be one which causes any damage to the organism itself, because, according to the method, the microorganism/cell would accumulate in the damaged tissue, and provide false readings, it would appear that the only methods of detection are by MRI or fluorescence detection. However, particular chromophores/fluorophores would not be reasonably predicted to detect tissues deep in the animal, and would necessarily be limited to surface tissues of the animal, e.g., SPECIFICATION, p. 10.

Conclusion

Because of the undue experimentation required to reasonably predict the working embodiments, the claimed invention would require the Artisan to perform undue experimentation, and hence, the claims are not enabled.

Response to Argument – Enablement

Applicant's argument of 12/18/06 has been fully considered but is not found persuasive.

Applicant argues that they have disclosed an envisioned invention, and therefore are enabled for such, providing their own analysis of the Wands factors (pp. 20-24).

Such is not persuasive. The analysis appears to be a proposed analysis to supplant that of the Examiner and fails to identify where in the Examiner's analysis the Examiner is incorrect, either by evidence or logic. Hence, it is not persuasive. Further, an envisioned invention is not enabled unless it does not require the Artisan to perform undue experimentation, which is that experimentation which would be required to invent the breadth of the subject matter claimed. The Examiner's analysis demonstrates that such is undue, and required for breadth of a large genera of disorders/diseases/microorganisms/bacteria as well as methods of detection. Hence, the claims are not enabled.

Applicant argues that Yu is post-filing art and thus, is not applicable, and further suggests that the Examiner should write a rejection for lack of operability (p. 24).

Such is not persuasive. Yu is what was known subsequent to Applicant's disclosure, and even at that point, the Art had not progressed to the point where bacterial/microorganism colonization was in any way predictable. Hence, before that point, even less was known. Given that even less was known, the Artisan would similarly find Applicant's disclosure even less reasonably predictable.

Applicant argues that the mechanism of colonization is irrelevant to the claimed invention, and therefore, they are enabled (p. 25).

Such is not persuasive. Without a mechanism to link Applicant's limited findings to the larger generas claimed, no extrapolation can be made to other bacteria/microorganisms, methods of administration, disorders and treatments, as well as when the bacteria/microorganism will colonize, and hence, the claims are not enabled for their breadth.

Applicant argues that they have amended the claims to remove separate detection steps of the microorganism/bacteria and the wound/tissues (pp. 25-26).

Such is persuasive. Hence, such aspect of enablement has been removed, however, the larger scope, to the core of the claimed invention is still not enabled for reasons of record.

Applicant broadly argues that the skill is high, and hence, the claims are enabled (p. 25).

Such is not persuasive. If such were true on its own, all claims in cell administration therapy would be inherently enabled. The fact is that the art cited is written by people of high skill, and they still do not know. High skill level would be a factor if it allowed the Art to be more reasonably predicted, but the Art, even to the Artisan is still not reasonably predictable.

Applicant argues that bacteriophages can localize to a wounded tissue, and the Examiner cannot take judicial notice to state such (pp. 26-27).

Such is not persuasive. First, the Examiner knows of no such prohibition of judicial notice. Second, in the context of the invention, the bacteriophage has to transform the cell and express the detectable protein, otherwise the DNA would not be expressed providing the signal. Third, if Applicant is relying on the fact that the present claims do not require expression of the DNA, there is no discussion in the specification of the bacteriophage containing, as part of its

protein coat, a protein which is detectable. Fourth, the Artisan would only understand the invention to have been drawn to bacteriophages which subsequently infect the tissue, express the protein, and such protein is detected. Fifth, it is a truism that bacteriophages do not infect eukaryotic cells. Sixth, if there is a lacking in an understanding of basic virology, please see the attached reference from http://www.answers.com/topic/bacteriophage. It is noted that such web page is post-filing date, but the Examiner takes official notice that such was also known in the Art prior to Applicant's filing date, as such was part of the Examiner's first biochemistry class in 1988.

Applicant broadly argues that the specification teaches many aspects of cells and administrations, and hence, the claims are enabled (pp. 27-28).

Such is not persuasive. It fails to demonstrate how the Examiner's reasoning is incorrect at all, but just demonstrates envisioned embodiments.

Applicant argues that the three specific examples provided, provide enough information for the Artisan to reasonably predict the scope of embodiments encompassed by the claims (pp. 28-29).

Such is not persuasive. Such does not provide any evidence or logical argument to demonstrate why the Examiner's reasoning is incorrect, or facts relied upon therein.

Applicant argues that the Examiner is misquoting Applicant with regard to the strain dependence and method of administration dependence of any bacteria/microorganism (p. 30).

Such is not persuasive. It is clear that the Examiner was not quoting Applicant, but paraphrasing, as the citation was not in quotes. Moreover, it is from Applicant's own examples, which demonstrate that even for the examples provided, it is not reasonably predictable.

Applicant argues that the statements made by the Examiner take the evidence out of context and demonstrate that the Examiner's argument is incorrect (p. 30).

Such is not persuasive. The bacteria have different distribution patterns, and arguments that the Artisan would know the distribution pattern are necessarily incorrect (i.e., distribution to the liver is to be expected), as it would necessarily require an analysis in control subjects to determine when, by any particular method of administration, the bacteria/microorganism is localized to the pertinent site. Essentially, the Artisan would have determine first whether it will colonize the various tissues, and further when it will colonize these tissues, and then determine if and when it will colonize the normal form of the tissue at the same time.

Applicant argues that Applicant never admitted that route of administration was important (pp. 31-32).

Such is not persuasive. The Examiner never stated such. Moreover, the evidence provided demonstrates that the route of administration influences the colonization. Its not reasonably predictable, and requires undue experimentation.

Applicant argues that accumulation in the liver would be known in the Art to not indicate or treat a condition (pp. 32-33).

Such is not persuasive. Applicant is arguing by their own argument that the claims are not enabled for liver. Second, when is the accumulation in the liver not diagnostic, and when is it diagnostic? The claims clearly cover liver tissue, as the specification contains discussion of detection of the bacteria/microorganism in the liver throughout, and no discussion of such tissue not being useful for such detection for any particular time period, or with any particular administration method.

Applicant argues that the colonization levels are important, and not the detection of bacteria/microorganisms itself (p. 33).

Such is not persuasive. The colonization level is not in the claims, the time frame when to detect such is not in the claims, and the argument itself is another supposition of how things may have occurred, proffered to supplant the Examiner's supposition, but does not demonstrate that the Examiner's analysis is incorrect.

Applicant argues that a particular level of efficacy is not required, and the claims are enabled (pp. 33-34).

Such is not persuasive. The Examiner is not arguing for a level of efficacy, but that given what is demonstrated, the Artisan cannot reasonably predict the huge breadth encompassed.

Applicant argues that the Examiner cannot take official notice, unless things are unquestionably deniable, and further the Examiner can demonstrate such (p. 34).

Such is not persuasive. The detection method may be extract the tissue, chop it up, and detect the DNA or mRNA therefrom, thereby detecting the tissue. Another method would be to cut open the tissue and see a marker protein, such as beta-galactosidase, change the color of X-gal. However, the processes of detection necessarily damages the tissue, and hence, demonstrates there will be colonization according to the method claimed.

Applicant argues broadly that the claims are enabled, because various steps are common with other methods known in the art (pp. 35-36).

Such is not persuasive. The steps may be used in the Art, but presumably, the method Applicant is attempting to claim is novel. If the Examiner is incorrect, please state such for the

record. However, the method is not enabled, regardless of whether people are injected with substances, or bacteria can emit light due to expression of a luciferase or fluorescent protein.

Applicant argues that the specification is not limited to disclosure of fluorescent proteins and MRI detection, as luminescent proteins are disclosed (p. 34).

Such is true, but Applicant has not limited the detection to fluorescent, luminescent and MRI detections only, but to any detection method, which apparently does not even require a signal to detect, which the Examiner further takes official notice is an impossibility.

Applicant argues that other methods of detection are available in the Art, including CT scans and PET scans (p. 34).

Such is persuasive. However, Applicant has not demonstrated how the Artisan would know, given the sparse disclosure, how to design a detectable microorganism/bacteria for these methods, and the Examiner does not understand how a fluorescent protein, encoded by a nucleic acid, would be detected in a CT scan.

Applicant rehashes their various arguments to conclude that the claims are enabled (pp. 38).

Such is not persuasive, as demonstrated in the arguments above.

Applicant argues policy considerations (pp. 38-39).

Such is not persuasive. The Examiner does not have any authority to overturn the law due to policy considerations. Further Applicant's argument of entitlement appears to agree with the Examiner's analysis, the Artisan would not find the claims enabled. Moreover, with regard to the invention being allowed for its breadth, the general argument the Examiner is making is that Applicant's claims are not a patentable invention, because they are not enabled.

Hence, the Claims remain and/or are newly rejected for lacking enablement.

The following rejections are made because of the breadth of the claims, even in light of the lack of enablement.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

In light of the amendments, the rejections of Claims 33-34, 36-37, 42-43, 57-62, and 69-72 under 35 U.S.C. 102(b) as being anticipated by Pace (2000) JAMA, 284(22): 2964, are withdrawn.

To wit, Streptococcus bacteria are pathogenic.

Conclusion

No Claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M. Kelly, Art Unit 1633, whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert M. Kelly, Ph.D.
Examiner, USPTO, AU 1633
Patents Hoteling Program
Mailbox 2C70, Remsen Building
(571) 272-0729

Joe Woitach
AU1633